

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Approval Package for:**

**Application Number**      **89489**

**Trade Name**   **Diphenhydramine Hydrochloride Capsules**  
**USP 50mg**

**Generic Name**   **Diphenhydramine Hydrochloride Capsules**  
**USP 50mg**

**Sponsor**      **Mutual Pharmaceutical Co, Inc.**

# **CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION      89489**

## **CONTENTS**

	<b>Included</b>	<b>Pending Completion</b>	<b>Not Prepared</b>	<b>Not Required</b>
<b>Approval Letter</b>	<b>X</b>			
<b>Tenative Approval Letter</b>				
<b>Approvable Letter</b>				
<b>Final Printed Labeling</b>	<b>X</b>			
<b>Medical Review(s)</b>				
<b>Chemistry Review(s)</b>	<b>X</b>			
<b>EA/FONSI</b>				
<b>Pharmacology Review(s)</b>				
<b>Statistical Review(s)</b>				
<b>Microbiology Review(s)</b>				
<b>Clinical Pharmacology Biopharmaceutics Review(s)</b>				
<b>Bioequivalence Review(s)</b>	<b>X</b>			
<b>Administrative Document(s)</b>	<b>X</b>			
<b>Correspondence</b>	<b>X</b>			

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Application Number**      **89489**

**APPROVAL LETTER**

ANDA 89-489

Mutual Pharmaceutical Company, Inc.  
Attention: Mr. Suhas Sardesai  
1100 Orthodox Street  
Philadelphia, Pennsylvania 19124

JAN 2 1987

Dear Mr. Sardesai:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Diphenhydramine Hydrochloride Capsules USP, 50 mg.

Also referenced is your communication of November 21, 1986.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved.

Any significant change in the conditions outlined in this abbreviated application requires an approved supplemental application before the change may be made, except for changes made in conformance with other provisions of Section 314.70 of the New Drug Regulations.

Postmarketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80 and 314.81 of the Regulations.

This Administration should be advised of any change in the marketing status of this drug.

**For Initial Campaigns:** We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your immediate advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Advertising and Labeling (HFN-240). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

**For Subsequent Campaigns:** We call your attention to Section 314.81(b)(5) of the Regulations which requires that materials for any subsequent advertising or promotional campaign, at the time of their initial use, be submitted to our Division of Drug Advertising and Labeling (HFN-240) with a completed Form FD-2253.

cc:

HFN-237

TPoux/CChang/MGoldman  
ved 12/18/86 (1515v)

APPROVAL

Sincerely yours,

Harvey Seife, M.D.

Director

Division of Generic Drugs  
Office of Drug Standards  
Center for Drugs and Biologics

2-19-86

1/2/87

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER**      **89489**

**FINAL PRINTED LABELING**



# Mutual Pharmaceutical Company, Inc.

1100 Orthodox Street • Philadelphia, Pennsylvania 19124 • (215) 288-6500

Labeling: **ORIGINAL**  
NDA No: 89489 AUG 27 1986  
Reviewed by: \_\_\_\_\_

12/16/86

<p>Each Capsule Contains: Diphenhydramine HCl, 50 mg USP</p> <p>Dispense in light container as de- lined in the USP. Store at controlled room temperature 15°-30°C (59°-86°F) Imprinted MUTUAL 107</p>	<p><b>EMPE</b></p> <p>NDC 53489-114-01 <b>DIPHENHYDRAMINE HCl CAPSULES, USP</b> 50 mg.</p> <p>CAUTION: Federal law prohibits dispensing without prescription. 100 CAPSULES</p> <p>MUTUAL PHARMACEUTICAL CO. INC. PHILADELPHIA, PA. 19124</p>	<p>Usual Dosage: see package insert</p> <p>Lot No: _____</p> <p>Exp Date: _____</p> <p>12/13/86</p>
<p>Each Capsule Contains: Diphenhydramine HCl, 50 mg USP</p> <p>Dispense in light container as de- lined in the USP. Store at controlled room temperature 15°-30°C (59°-86°F) Imprinted MUTUAL 107</p>	<p><b>EMPE</b></p> <p>NDC 53489-114-01 <b>DIPHENHYDRAMINE HCl CAPSULES, USP</b> 50 mg.</p> <p>CAUTION: Federal law prohibits dispensing without prescription. 100 CAPSULES</p> <p>MUTUAL PHARMACEUTICAL CO. INC. PHILADELPHIA, PA. 19124</p>	<p>Usual Dosage: see package insert</p> <p>Lot No: _____</p> <p>Exp Date: _____</p> <p>12/13/86</p>
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# Mutual Pharmaceutical Company, Inc.

1100 Orthodox Street • Philadelphia, Pennsylvania 19124 • (215) 288-6500

12/18/86

Each Capsule Contains:  
Diphenhydramine HCl, USP ..... 50 mg.  
Dispense in light container as defined in the USP.  
Store at controlled room temperature  
15°-30°C (59°-86°F).  
Imprinted MUTUAL  
107

**EMPE**  
NDC 53489-114-10  
**DIPHENHYDRAMINE HCl  
CAPSULES, USP**  
**50 mg.**  
CAUTION: Federal law prohibits  
dispensing without prescription.  
**1000 CAPSULES**

MUTUAL PHARMACEUTICAL CO., INC.  
PHILADELPHIA, PA. 19124

Usual Dosage: see package insert.  
Lot No:   
Exp. Date:   
12/18/86

Each Capsule Contains:  
Diphenhydramine HCl, USP ..... 50 mg.  
Dispense in light container as defined in the USP.  
Store at controlled room temperature  
15°-30°C (59°-86°F).  
Imprinted MUTUAL  
107

**EMPE**  
NDC 53489-114-10  
**DIPHENHYDRAMINE HCl  
CAPSULES, USP**  
**50 mg.**  
CAUTION: Federal law prohibits  
dispensing without prescription.  
**1000 CAPSULES**

MUTUAL PHARMACEUTICAL CO., INC.  
PHILADELPHIA, PA. 19124

Usual Dosage: see package insert.  
Lot No:   
Exp. Date:   
12/18/86

Each Capsule Contains:  
Diphenhydramine HCl, USP ..... 50 mg.  
Dispense in light container as defined in the USP.  
Store at controlled room temperature  
15°-30°C (59°-86°F).  
Imprinted MUTUAL  
107

**DIPHENHYDRAMINE HCl  
CAPSULES, USP**  
**50 mg.**  
CAUTION: Federal law prohibits  
dispensing without prescription.  
**1000 CAPSULES**

MUTUAL PHARMACEUTICAL CO., INC.  
PHILADELPHIA, PA. 19124

Usual Dosage: see package insert.  
Lot No:   
Exp. Date:   
12/18/86

Labeling: ORIGINAL

NDA No: \_\_\_\_\_ Rev'd. AUG 27 1986

Reviewed by: \_\_\_\_\_

**DOSAGE AND ADMINISTRATION:** DOSAGE SHOULD BE INDIVIDUALIZED ACCORDING TO THE NEEDS AND THE RESPONSE OF THE PATIENT.

A single oral dose of diphenhydramine hydrochloride is quickly absorbed with maximum activity occurring in approximately one hour. The duration of activity following an average dose of diphenhydramine hydrochloride is from four to six hours.

**ADULTS:** 25 to 50 mg three to four times daily. The nighttime sleep-aid dosage is 50 mg at bedtime.

**CHILDREN:** (over 20 lb): 12.5 to 25 mg three or four times daily. Maximum daily dosage not to exceed 300 mg. For physicians who wish to calculate the dose on the basis of body weight or surface area, the recommended dosage is 5mg/kg/24 hours or 150 mg/m<sup>2</sup>/24 hours.

Data are not available on the use of diphenhydramine hydrochloride as a nighttime sleep-aid in children under 12 years.

The basis for determining the most effective dosage regimen will be the response of the patient to medication and the condition under treatment.

In motion sickness, full dosage is recommended for prophylactic use, the first dose to be given 30 minutes before exposure to motion and similar doses before meals and upon retiring for the duration of exposure.

#### HOW SUPPLIED

**DIPHENHYDRAMINE HYDROCHLORIDE** Capsules are supplied as follows:

**DIPHENHYDRAMINE HYDROCHLORIDE** 25 mg Pink/Clear capsules, Imprinted MUTUAL 103.

Bottles of 100, NDC 53489-113-01  
Bottles of 1000, NDC 53489-113-10

**DIPHENHYDRAMINE HYDROCHLORIDE** 50 mg Pink/Pink capsules, Imprinted MUTUAL 107.

Bottles of 100, NDC 53489-114-01  
Bottles of 1000, NDC 53489-114-10

**STORAGE CONDITIONS:** Store at controlled room temperature 15°-30°C (59°-86°F). Protect from moisture.

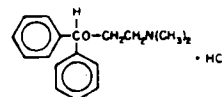
Caution — Federal law prohibits dispensing without prescription.

Manufactured by:  
**MUTUAL PHARMACEUTICAL COMPANY, INC.**  
Philadelphia, PA 19124

Issued: August 1986

## DIPHENHYDRAMINE HYDROCHLORIDE CAPSULES, USP

**DESCRIPTION:** Diphenhydramine hydrochloride is an antihistamine drug having the chemical name 2-(Diphenylmethoxy)-N,N-dimethylethylamine hydrochloride and has the empirical formula C<sub>17</sub>H<sub>21</sub>NO·HCl (molecular weight 291.82). It occurs as a white, crystalline powder and is freely soluble in water and alcohol. The structural formula is as follows:



Each diphenhydramine hydrochloride capsule contains 25 mg or 50 mg diphenhydramine hydrochloride for oral administration.

**CLINICAL PHARMACOLOGY:** Diphenhydramine hydrochloride is an antihistamine with anticholinergic (drying) and sedative effects. Antihistamines appear to compete with histamine for cell receptor sites on effector cells.

A single oral dose of diphenhydramine hydrochloride is quickly absorbed with maximum activity occurring in approximately one hour. The duration of activity following an average dose of diphenhydramine hydrochloride is from four to six hours. Diphenhydramine is widely distributed throughout the body, including the CNS. Little, if any, is excreted unchanged in the urine; most appears as the degradation products of metabolic transformation in the liver, which are almost completely excreted within 24 hours.

**INDICATIONS AND USAGE:** Diphenhydramine hydrochloride in the oral form is effective for the following indications:

**Antihistaminic:** For allergic conjunctivitis due to foods; mild, uncomplicated allergic skin manifestations of urticaria and angioedema; amelioration of allergic reactions to blood or plasma; dermatographism; as therapy for anaphylactic reactions adjunctive to epinephrine and other standard measures after the acute manifestations have been controlled.

**Motion sickness:** For active and prophylactic treatment of motion sickness.

**Antiparkinsonism:** For parkinsonism (including drug-induced) in the elderly.



unable to tolerate more potent agents; mild cases of parkinsonism (including drug-induced) in other age groups; in other cases of parkinsonism (including drug-induced) in combination with centrally acting anticholinergic agents.

Nighttime sleep-aid.

#### CONTRAINDICATIONS

**Use In Newborn or Premature Infants:** This drug should not be used in newborn or premature infants.

**Use In Nursing Mothers:** Because of the higher risk of antihistamines for infants generally, and for newborns and prematures in particular, antihistamine therapy is contraindicated in nursing mothers.

Antihistamines are also contraindicated in the following conditions:

Hypersensitivity to diphenhydramine hydrochloride and other anti-histamines of similar chemical structure.

**WARNINGS:** Antihistamines should be used with considerable caution in patients with narrow-angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, symptomatic prostatic hypertrophy, or bladder-neck obstruction.

**Use In Children:** In infants and children, especially, antihistamines in overdosage may cause hallucinations, convulsions, or death.

As in adults, antihistamines may diminish mental alertness in children. In the young child, particularly, they may produce excitation.

**Use in the Elderly (approximately 60 years or older):** Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients.

#### PRECAUTIONS

**General:** Diphenhydramine hydrochloride has an atropine-like action and therefore should be used with caution in patients with a history of lower respiratory disease including asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease or hypertension.

**Information for Patients:** Patients taking diphenhydramine hydrochloride should be advised that this drug may cause drowsiness and has an additive effect with alcohol.

Patients should be warned about engaging in activities requiring mental alertness such as driving a car or operating appliances, machinery, etc.

**Drug Interactions:** Diphenhydramine hydrochloride has additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc).

MAO inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Long-term studies in animals to determine mutagenic and carcinogenic potential have not been per-

formed.

**Pregnancy:** Pregnancy Category B. Reproduction studies have been performed in rats and rabbits at doses up to 5 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to diphenhydramine hydrochloride. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

**ADVERSE REACTIONS:** The most frequent adverse reactions are underscored.

1. **General:** Urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills, dryness of mouth, nose, and throat
2. **Cardiovascular System:** Hypotension, headache, palpitations, tachycardia, extrasystoles
3. **Hematologic System:** Hemolytic anemia, thrombocytopenia, agranulocytosis
4. **Nervous System:** Sedation, sleepiness, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesia, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, neuritis, convulsions
5. **GI System:** Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation
6. **GU System:** Urinary frequency, difficult urination, urinary retention, early menses
7. **Respiratory System:** Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness

**OVERDOSAGE:** Antihistamine overdosage reactions may vary from central nervous system depression to stimulation. Stimulation is particularly likely in children. Atropine-like signs and symptoms, dry mouth; fixed, dilated pupils; flushing, and gastrointestinal symptoms may also occur.

If vomiting has not occurred spontaneously the patient should be induced to vomit. This is best done by having him drink a glass of water or milk after which he should be made to gag. Precautions against aspiration must be taken, especially in infants and children.

If vomiting is unsuccessful gastric lavage is indicated within 3 hours after ingestion and even later if large amounts of milk or cream were given beforehand. Isotonic or 1/2 isotonic saline is the lavage solution of choice.

**Saline cathartics**, as milk of magnesia, by osmosis draw water into the bowel and therefore are valuable for their action in rapid dilution of bowel content

**Stimulants** should not be used.

Vasopressors may be used to treat hypotension.

100  
2 1987

12/8/86

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER      89489**

**CHEMISTRY REVIEW(S)**

CHEMIST'S REVIEW ANDA 89-489

3. NAME AND ADDRESS OF APPLICANT

Mutual Pharmaceutical Company, Inc.  
Philadelphia, PA 19124

7. NONPROPRIETARY NAME

Diphenhydramine Hydrochloride

10. PHARMACOLOGICAL CATEGORY

Antihistamine

11. HOW DISPENSED

Rx

12. RELATED IND/NDA/DMF(s)

89-488 (25 mg)

89-489 (50 mg)

13. DOSAGE FORM(s)

Capsule

14. POTENCY

50 mg

15. CHEMICAL NAME AND STRUCTURE

Name and structure same as USP XXI (need italics for -N-N-).

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

Approvable

19. REVIEWER:

MGoldman

DATE COMPLETED:

12/17/86

12/18/86

CHEMIST'S REVIEW ANDA 89-489

3. NAME AND ADDRESS OF APPLICANT

Mutual Pharmaceutical Company, Inc.  
Philadelphia, PA 19124

7. NONPROPRIETARY NAME

Diphenhydramine Hydrochloride

10. PHARMACOLOGICAL CATEGORY

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11. HOW DISPENSED

Rx

12. RELATED IND/NDA/DMF(s)

89-488 (25 mg)

89-489 (50 mg)

13. DOSAGE FORM(s)

Capsule

14. POTENCY

50 mg

15. CHEMICAL NAME AND STRUCTURE

Name and structure same as USP XXI.

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

Not Approvable

19. REVIEWER:

MGoldman

DATE COMPLETED:

10/30/89

3. NAME AND ADDRESS OF APPLICANT

Mutual Pharmaceutical Company, Inc.  
Philadelphia, PA 19124

7. NONPROPRIETARY NAME

Diphenhydramine Hydrochloride

10. PHARMACOLOGICAL CATEGORY

Antihistamine

11. HOW DISPENSED

Rx

12. RELATED IND/NDA/DMF(s)

89-488 (25 mg)  
89-489 (50 mg)

13. DOSAGE FORM(s)

Capsule

14. POTENCY

50 mg

15. CHEMICAL NAME AND STRUCTURE

Name and structure same as USP-XXI (need italics for -N-N-).

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

Not Approvable

19. REVIEWER:

MGoldman

DATE COMPLETED:

10/8/86

20. COMPONENTS AND COMPOSITION

<u>Component</u>	<u>Reference</u>	<u>mg/capsule</u>
Diphenhydramine HCl	USP	50.0
Starch, NF	NF	
Magnesium Stearate	NF	
	TOTAL	<u>200.0 mg</u>

Components of capsule not given. See page 97.

CHEMIST'S REVIEW ANDA 89-489

3. NAME AND ADDRESS OF APPLICANT

Mutual Pharmaceutical Company, Inc.  
Philadelphia, PA 19124

7. NONPROPRIETARY NAME

Diphenhydramine Hydrochloride

10. PHARMACOLOGICAL CATEGORY

Antihistamine

11. HOW DISPENSED

Rx

12. RELATED IND/NDA/DMF(s)

89-488 (25 mg)  
89-489 (50 mg)

13. DOSAGE FORM(s)

Capsule

14. POTENCY

50 mg

15. CHEMICAL NAME AND STRUCTURE

Name and structure same as USP XXI (need italics for -N-N-).

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

Not Approvable

19. REVIEWER:

MGoldman

DATE COMPLETED:

9/11/86

20. COMPONENTS AND COMPOSITION

<u>Component</u>	<u>Reference</u>	<u>mg/capsule</u>
Diphenhydramine HCl	USP	50.0
Starch, NF	NF	
Magnesium Stearate	NF	
TOTAL		200.0 mg

Components of capsule not given. See page 97.  
Botanical source of Starch not given.

CHEMIST'S REVIEW ANDA 89-489

3. NAME AND ADDRESS OF APPLICANT

Mutual Pharmaceutical Company, Inc.  
Philadelphia, PA 19124

7. NONPROPRIETARY NAME

Diphenhydramine Hydrochloride

10. PHARMACOLOGICAL CATEGORY

Antihistamine

11. HOW DISPENSED

Rx

12. RELATED IND/NDA/DMF(s)

89-488 (25 mg)  
89-489 (50 mg)

13. DOSAGE FORM(s)

Capsule

14. POTENCY

50 mg

15. CHEMICAL NAME AND STRUCTURE

Name and structure same as USP XXI (need italics for -N-N-).

17. COMMENTS

18. CONCLUSIONS AND RECOMMENDATIONS

Not Approvable

19. REVIEWER:

MGoldman

DATE COMPLETED:

7/29/86

20. COMPONENTS AND COMPOSITION

<u>Component</u>	<u>Reference</u>
Diphenhydramine HCl	USP
Starch, NF	NF
Magnesium Stearate	NF

Components of capsule not given. See page 97.

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER      89489**

**BIOEQUIVALENCE REVIEW(S)**



NDA 89-489  
89-489

Mutual Pharmaceutical Co. Inc.  
Attention: Suhns Sardesai  
1100 Orthodox Street  
Philadelphia, PA 19124

Dear Sir:

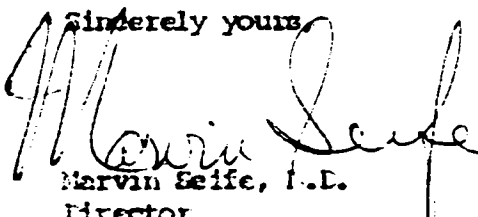
Reference is made to the dissolution data and request for waiver of in-vivo bioavailability requirements you submitted on May 9, 1986 for Diphenhydramine Hydrochloride Capsules, 25 mg.

The data and your request have been reviewed by our Division of Bioequivalence and they have the following comments:

- "1. The dissolution testing conducted by Mutual Pharmaceutical Co. Inc. on its Diphenhydramine HCl Capsules, 25 mg and 50 mg, is acceptable. The waiver of the in-vivo bioequivalence study requirements for the 25 mg and 50 mg Diphenhydramine HCl Capsule is granted. The 25 mg and 50 mg capsule of the test product is therefore deemed bioequivalent to the 25 mg and 50 mg capsule, respectively, of Benadryl, manufactured by Parke-Davis Co.
2. The dissolution testing should be incorporated into your manufacturing controls and stability program. The dissolution testing should be conducted in 500 ml. of water @ 37°C using U.S.P. XXI Apparatus I (Basket) at 100 rpm. The test product should meet the following specification:

Not less than      of the labeled amount of the drug  
in the dosage form is dissolved in 45 minutes."

Sincerely yours

 12/2/86  
Marvin Seife, I.D.  
Director  
Division of Generic Drugs  
Office of Drug Standards  
Center for Drugs and Biologics

cc: IFN-230  
Goldman  
MSeife/JSturm/jt/12-2-86  
BIO 0530b

Diphenhydramine HCl  
50 mg. Capsule  
ANDA #89-489  
Reviewer: Ramona D. McCarthy  
Wang # 8982e

Mutual Pharmaceutical Co., Inc.  
Philadelphia, Pennsylvania  
Submission Dated:  
May 9, 1986

Review of Dissolution Data and A Request For A Waiver  
of The In-Vivo Bioequivalence Requirement

The firm submitted comparative dissolution data on both the test product and the reference product, Benadryl (diphenhydramine HCl) Capsules, 50 mg. The data demonstrate that the product meets our specifications of N.L.T. of the drug in the dosage form dissolved in 45 minutes.

This submission also contains a request for a waiver of the in-vivo bioequivalence requirement for this product.

This composition of this product is as follows:

<u>Component</u>	<u>mg/Capsule</u>
Diphenhydramine HCl, U.S.P.	50.0 mg
Starch, N.F.	
Magnesium Stearate, N.F.	

Comment

In as much as the reference product Benadryl (diphenhydramine HCl) has been determined to be effective for at least one indication in a D.E.S.I. notice and this product is basically the same product, this product meets the criteria necessary to meet the requirements of C.F.R. 320.22(C)(1). Accordingly, a waiver may be granted and the firm should be so advised.

Recommendation

The firm should be advised as follows:

1. The dissolution testing conducted by Mutual Pharmaceutical Co. Inc. on its diphenhydramine HCl Capsules, 50 mg., Lot #10060, is acceptable. The waiver of the in-vivo bioequivalence study requirements for the 50 mg. Diphenhydramine HCl Capsule is granted. The 50 mg. capsule of the test product is therefore deemed bioequivalent to the 50 mg. capsule of Benadryl, manufactured by Parke-Davis Co.
2. The dissolution testing should be incorporated into the firm's manufacturing controls and stability program. The dissolution testing should be conducted in 500 ml. of water @ 37°C using U.S.P.XXI Apparatus I (Basket) at 100 rpm. The test product should meet the following specification:

Not less than        of the labeled amount of the drug  
in the dosage form is dissolved in 45 minutes.

Ramona D. McCarthy  
Division of Bioequivalence  
Review Branch 1

RD INITIALED BY AJACKSON  
FT INITIALED BY AJACKSON

Concur: \_\_\_\_\_  
S.V. Dighe  
Director  
Division of Bioequivalence

Date: 11-21-86

R.McCarthy/do/11-10-86/Wang #8982e

cc: ANDA #89-489 original (2) HFN-230, HFN-200 (Hare),  
HFN-223 (Shah), HFN-252 (McCarthy, Jackson) Drug File

Generic Name: Diphenhydramine HCl Capsule Firm Name: Mutual Pharmaceutical

Trade Name: \_\_\_\_\_

Firm Location: Philadelphia, Penna

Dosage: 25 mg

Submission Date: May 9, 1986

ANDA #: 89-488

Reviewer: \_\_\_\_\_

Hang # 89812

#### REVIEW OF DISSOLUTION DATA

Objective of Submission: Compliance with Bioavailability/Bio-  
equivalence Requirement Guidelines for a NDA  
Approval. Comparative dissolution testing data  
submitted on both test and reference products.

#### Condition for Dissolution Testing

USP XX Apparatus Paddle \_\_\_\_\_ Basket ☒ RPM 100

Medium: Water Volume 500 ml

Number of Tab/Capsules Tested: 12

Reference Drug: Benadryl (diphenhydramine HCl) Parke-Davis

Assay Methodology

Results *Mictural*  
*Diphenhydramine HCL 25mg*  
Time TEST PRODUCT

**fine**

## Final Product

Lot # 10069

## Mean % Dissolved

## Range

(CV)

*Benadryl (P.O.)*  
*(diphenhydramine HCl)*  
Reference Product

Lot # 034554

Mean %  
Dissolved

## Range

(CV)

Time	Temp	Time	Temp	Time	Temp
15 min	87.43	16.23	103.15		(1.28)
30 "	100.81	3.59	102.89		(1.06)
45 "	101.81	3.06	103.13		(1.03)
60 "	103.10	2.13	102.05		(1.32)
90 "	102.82	3.00	102.44		(2.36)
		( )			( )
		( )			( )
		( )			( )
		( )			( )
		( )			( )

Lot #

Lot # \_\_\_\_\_

[illegible]

Generic Name: Diphenhydramine HCl

Firm Name: Mutual Pharmaceutical Co.

Trade Name: \_\_\_\_\_

Firm Location: Philadelphia, Penna.

Dosage: 50mg

Submission Date: May 9, 1986

ANDA #: 89-489

Reviewer: \_\_\_\_\_

Wang # \_\_\_\_\_

### REVIEW OF DISSOLUTION DATA

Objective of Submission: Compliance with Bioavailability / Bio-  
equivalence Requirement Guidelines for ANDA  
Approval. Comparative dissolution testing data sub-  
mitted on both test and reference products.

### Condition for Dissolution Testing

USP XI Apparatus Paddle \_\_\_\_\_

Basket ☒

RPM

100

Medium: Water

Volume

500

ml

Number of Tab/Capsules Tested: 12

Reference Drug: Benadryl (diphenhydramine HCl) Parke-Davis

Assay Methodology



**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER**                      **89489**

**ADMINISTRATIVE DOCUMENTS**



# ANDA Approval Summary

89-489

NDA Number

Mutual Pharm. Co.

Applicant Name

Diphenhydramine HCl

Established Name of Drug

Capsula

Dosage Form

50mg

Strength

100's 1000's

Container size(s)

Date Found Satisfactory

Comment

Labeling

12/16/86

Chemistry, Manufacturing, and Controls

12/16/86

MP's

Manufacturer - Finished Dosage Form

12/16/86

Outside Facilities

12/16/86

Manufacturer(s) - Active Ingredient(s)

12/16/86

Chemist Reviewer

Date

12/16/86

Date

Patent Information Required

X

No

Yes

Patent Drug Information 505(j)(2)(A)

Acceptable see 5/9/86 submission

Patent Certification 505(j)(2)(A)

1

1

Patent/Exclusivity Expires (if applicable)

N/A

Bioequivalence Section

Dissolution Required?

No

Yes

DB

DGD

Acceptable see 12/3/86 Ltr

In vivo study(s) required?

No

Yes

THIS IS AN AA Drug  
THERE IS NO IN VIVO REQUIREMENT

Study(s) Found Acceptable

Waiver Request Granted

Waiver Granted see 12/3/86 Ltr

Total Bioequivalence Requirement Met

See above

Administrative Reviewer

Date

Approved

Disapproved

Comments:

Director, Division of Generic Drugs

Date

<b>NOTICE OF APPROVAL</b> <b>NEW DRUG APPLICATION OR SUPPLEMENT</b>		NDA NUMBER <div style="text-align: center;">89-489</div>
TO:  <div style="text-align: center;">Press Relations Staff (HF1-40)</div>		FROM:  <input checked="" type="checkbox"/> Bureau of Drugs  <input type="checkbox"/> Bureau of Veterinary Medicine
<b>ATTENTION</b> Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.		
TYPE OF APPLICATION <input type="checkbox"/> ORIGINAL NDA <input type="checkbox"/> SUPPLEMENT TO NDA <input checked="" type="checkbox"/> ABBREVIATED ORIGINAL NDA <input type="checkbox"/> SUPPLEMENT TO ANDA		CATEGORY <input checked="" type="checkbox"/> HUMAN <input type="checkbox"/> VETERINARY
TRADE NAME (or other designated name) AND ESTABLISHED OR NONPROPRIETARY NAME (if any) OF DRUG <div style="text-align: center;">Diphenhydramine Hydrochloride</div>		
DOSAGE FORM <div style="text-align: center;">Capsule</div>		HOW DISPENSED <input checked="" type="checkbox"/> RX <input type="checkbox"/> OTC
ACTIVE INGREDIENT(S) (as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)  <div style="text-align: center;">Diphenhydramine Hydrochloride, 50 mg</div>		
NAME OF APPLICANT (Include City and State) <div style="text-align: center;">Mutual Pharmaceutical Co., Inc. 1100 Orthodox Street Philadelphia, PA 19124</div>		
PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY <div style="text-align: center;">Antihistamine</div>		
COMPLETE FOR VETERINARY ONLY		
ANIMAL SPECIES FOR WHICH APPROVED		
COMPLETE FOR SUPPLEMENT ONLY		
CHANGE APPROVED TO PROVIDE FOR		
FORM PREPARED BY NAME <u>M. Goldman</u>		DATE <u>12/1/88</u>
FORM APPROVED BY NAME <u>C. Chang</u>		DATE <u>12/1/88</u>



DEPARTMENT OF HEALTH & HUMAN SERVICES

M. GOLDMAN

Memorandum

TO : Manufacturing Review Branch (HFN-324)  
Division of Drug Quality Compliance

DATE: 5/16/86

FROM : Division of Generic Drugs  
Requester's Name Diane F. Walker

PHONE: 443-0193

SUBJECT: ESTABLISHMENT EVALUATION REQUEST

NDA, ANDA, AND SUPPLEMENT NUMBER: 89-488; 89-489

DRUG TRADE MARK (if any)

DRUG NONPROPRIETARY NAME: Diphenhydramine Hydrochloride Capsules USP, 25 mg;

50 mg  
DOSAGE FORM AND STRENGTH(S): CHG

DRUG CLASSIFICATION:  
(Priority) A or B 1C Other

PROFILE CLASS CODE:

APPLICANT'S NAME: Mutual Pharmaceutical Co.

ADDRESS: 1100 Orthodox St., Philadelphia, PA

FACILITIES TO BE EVALUATED: (Name, Full Address, DMF# (if any), and Responsibility)

- 1. applicant - mfr finished dosage form

cc: HFC-121 narrow

Co

Re:

\*\*\*\*\*  
FOR HFN-324 USE ONLY:

Request Rec'd: 5/24/86

Inspection Requested:  
(if applicable)

Firm(s) are in Compliance With GMPs: acceptable

Basis for Determination:  
Reviewing C

6/24/86 Concurrence:

cc: HFN-234  
HFN-  
HFN-324

ANDA ADMINISTRATIVE CONTROL RECORD

Applicant Mylan Pharmaceuticals

ANDA # 59459

Date Recd. 5/13/86

Trade Name \_\_\_\_\_

RX ☒ OTC \_\_\_\_\_

Generic Name/Dosage Form/Strength: Diphenhydramine

Hydrochloride Capsules USP, 25 mg

DESI Drug \_\_\_\_\_

Similar or Related \_\_\_\_\_

Applicant Manufacturer: Yes ☒ No \_\_\_\_\_

If No: Name of Manufacturer \_\_\_\_\_

ANDA # \_\_\_\_\_ Approved: \_\_\_\_\_ Pending \_\_\_\_\_ Same Formulation \_\_\_\_\_

Application Complete YES ☒

NO \_\_\_\_\_

Application Acceptable: YES ☒

NO \_\_\_\_\_

*Has info on  
just OTC*

Letter to Firm: Acknowledgement: ☒ Not-acceptable \_\_\_\_\_ Date 5/13/86

CSO/CST: \_\_\_\_\_ Date 5/16/86

BIO Review Required: YES ☒ NO \_\_\_\_\_ IN VITRO ☒ IN VIVO \_\_\_\_\_

Medical Officer \_\_\_\_\_

Chemist \_\_\_\_\_

Inspection Request to HFD 320 (Date): 5/16/86

S 9-487

## ANDA CHECKLIST FOR COMPLETENESS AND ACCEPTABILITY OF THE APPLICATION

	<u>Yes</u>	<u>No</u>
Letter _____	✓	
356H Signed _____	✓	
Table of Contents _____	✓	
Information to show proposed product is same as listed product: (i) indications (ii) active ingredients (iii) (a) route (b) dosage form (c) strength (iv) labeling _____	✓	
Patent Certification _____	✓	
Exclusivity Addressed (If Applicable) _____		
Labeling _____	Draft	
Statement re Rx/OTC Status _____	✓	
Components & Composition (Unit Composition) _____	✓	
Manufacturing Controls _____	✓	
Batch Formulation _____	✓	
Certification of GMP _____	✓	
Description of Facilities _____	✓	
Manufacturing Procedures (Batch Records) _____	✓	
Specs & Tests for Active Ingredient and Finished Dosage Form _____	✓	
Stability Profile Including Stability Data (Use of Stability Indicating Method) _____	✓	
Samples Statement Plus Data _____		
Bioavailability/Bioequivalence Protocol _____		
Study _____		
In vivo study/waiver request _____	✓	
Dissolution Data _____	✓	
Environmental Impact Analysis _____	✓	



DEPARTMENT OF HEALTH & HUMAN SERVICES

Memorandum

TO :Manufacturing Review Branch (HFN-322)  
Division of Drug Quality Compliance

DATE: 5/16/86

FROM :Division of Generic Drugs

Requester's Name Diane F. Walker

PHONE: 443-0193

SUBJECT: ESTABLISHMENT EVALUATION REQUEST

NDA, ANDA, AND SUPPLEMENT NUMBER: 89-488; 89-489

DRUG TRADE MARK (if any)

DRUG NONPROPRIETARY NAME: Diphenhydramine Hydrochloride Capsules USP, 25 mg;

50 mg  
DOSAGE FORM AND STRENGTH(S): CHG

DRUG CLASSIFICATION:

(Priority)

A or B

1C

Other

PROFILE CLASS CODE:

APPLICANT'S NAME: Mutual Pharmaceutical Co.

ADDRESS: 1100 Orthodox St., Philadelphia, PA

FACILITIES TO BE EVALUATED: (Name, Full Address, DMF# (if any), and Responsibility)

1. applicant - mfr finished dosage form

cc: HFC-13. J. Darrow

Comm

Reas

\*\*\*\*\*  
FOR HFN-322 USE ONLY:

Request Rec'd: \_\_\_\_\_

Inspection Requested: \_\_\_\_\_  
(if applicable)

Firm(s) are in Compliance With GMPs: \_\_\_\_\_

Basis for Decision: \_\_\_\_\_

Reviewing CSO: \_\_\_\_\_

Concurrence: \_\_\_\_\_

cc: HFN-\_\_\_\_\_  
HFN-\_\_\_\_\_  
HFN-322

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER      89489**

**CORRESPONDENCE**

ANDA 89-489

Mutual Pharmaceutical Company, Inc.

Attention: Suhas Sardesai

1100 Orthodox Street

Philadelphia, PA 19124

Dear Mr. Sardesai:

Please refer to your abbreviated new drug application dated May 9, 1986, submitted pursuant to Section 505 of the Federal Food, Drug, and Cosmetic Act for Diphenhydramine Hydrochloride Capsules USP, 50 mg.

Also referenced is your communication of October 14, 1986.

The application is deficient and therefore not approvable under Section 505 of the Act for the following reasons:

1. Your comparative dissolution rate studies and request for bioavailability/bioequivalency waiver is under review by the Division of Bioequivalence. You will be advised when their review is completed.
2. For the Components and Composition sections:  
21 CFR 314.50(d)(ii) Drug Product requires that you provide "A list of all components used in the manufacture of the drug product (regardless of whether they appear in the drug product); and a statement of the composition of the drug product. . ." You must submit a revised Component Section 6 and revised Composition Section 7 which lists all ingredients of the drug products, including the capsule. The container need not be included.
3. We acknowledge withdrawal of as a testing laboratory.

The file is now closed. You are required to take one of the actions described at 21 CFR 314.120 which will either amend or withdraw the application, or if you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

for  
11-3-86  
Marvin Seife, M.D.  
Director  
Division of Generic Drugs  
Office of Drug Standards  
Center for Drugs and Biologics

CC:

HFN-237

TPoux/CChang/MGoldman/tr/10/30/86

1032S

Not Approvable



ANDA 89-489

Mutual Pharmaceutical Company, Inc.  
Attention: Suhas Sardesai  
1100 Orthodox Street  
Philadelphia, PA 19124

OCT 10 1986

Dear Mr. Sardesai:

Please refer to your abbreviated new drug application dated May 9, 1986, submitted pursuant to Section 505 of the Federal Food, Drug, and Cosmetic Act for Diphenhydramine Hydrochloride Capsules USP, 50 mg.

Also referenced is your communication of September 19, 1986.

The application is deficient and therefore not approvable under Section 505 of the Act for the following reasons:

1. Your comparative dissolution rate studies and request for bioavailability/bioequivalency waiver is under review by the Division of Bioequivalence. You will be advised when their review is completed.
2. For the Components and Composition sections:  
You must provide a copy of your revised Component section and your revised Composition section showing the formula for the capsule shell, whose ingredients are shown on page 97 of your original application.
3. is at present unacceptable as a testing laboratory for the active ingredient, starch, and magnesium stearate. Please indicate your intentions with respect to use of this firm.

The file is now closed. You are required to take one of the actions described at 21 CFR 314.120 which will either amend or withdraw the application, or if you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours

Marvin Seife, M.D.  
Director  
Division of Generic Drugs  
Office of Drug Standards  
Center for Drugs and Biologics

cc:

HFN-237

TPoux/CChang/MGoldman/tr/10/8/86

1032S

Not Approvable

2/10-9-86

10/5/86

1802

10-10-86

ANDA 89-489

SEP 15 1986

Mutual Pharmaceutical Company, Inc.  
Attention: Suhas Sardesai  
1100 Orthodox Street  
Philadelphia, PA 19124

Dear Mr. Sardesai:

Please refer to your abbreviated new drug application dated May 9, 1986, submitted pursuant to Section 505 of the Federal Food, Drug, and Cosmetic Act for Diphenhydramine Hydrochloride Capsules USP, 50 mg.

Also referenced is your communication of August 26, 1986.

The application is deficient and therefore not approvable under Section 505 of the Act for the following reasons:

1. Your comparative dissolution rate studies and request for bioavailability/bioequivalency waiver is under review by the Division of Bioequivalence. You will be advised when their review is completed.

2. For the Components and Composition sections:

You must provide a copy of your revised Component section and your revised Composition section showing the following:

- a. The formula for the capsule.
- b. The botanical source of the starch, as required by the NF.

3. For the active ingredient:

Provide complete name and address for

4. It fails to provide rework (reprocessing) procedures used in the event a batch fails to meet specifications (page 131), as required by 21 CFR 211.115.

The file is now closed. You are required to take one of the actions described at 21 CFR 314.120 which will either amend or withdraw the application, or if you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

FOR

9-15-86

CC:  
HFN-23,

TPoux/Cchang/MGoldman/tr/9/11/86  
1032S

Not Approvable

Marvin Seife, M.D.  
Director  
Division of Generic Drugs  
Office of Drug Standards  
Center for Drugs and Biologics



# Mutual Pharmaceutical Company, Inc.

1100 Orthodox Street • Philadelphia, Pennsylvania 19124 • (215) 288-6500

August 26, 1986

Marvin Seife, M.D.  
Director  
Division of Generic Drugs  
Office of Drug Standards  
Center for Drugs and Biologics  
Food and Drug Administration  
HFN 230, Rm 17B - 20  
5600 Fishers Lane  
Rockville, MD 20857

ANDA ORIG. AMENDMENT

FPL

Re: ANDA 89-489, Amendment A01  
Product: Diphenhydramine HCl Capsules USP, 50 mg.

Dear Dr. Seife:

In pursuant to the communication dated July 31, 1986, in which there is stated some deficiencies in our original application; we are herewith submitting the necessary corrections.

We respectfully request that you re-open our file.

Sincerely,

Suhas Sardesai

Suhas Sardesai, MS  
Director of Operations

lcp

cc

enclosure

RECEIVED  
AUG 27 1986  
GENERIC DRUGS

ANDA 89-489

Mutual Pharmaceutical Company, Inc.  
Attention: Suhas Sardesai  
1100 Orthodox Street  
Philadelphia, PA 19124

JUL 31 1986

Dear Mr. Sardesai:

Please refer to your abbreviated new drug application dated May 9, 1986, submitted pursuant to Section 505 of the Federal Food, Drug, and Cosmetic Act for Diphenhydramine Hydrochloride Capsules USP, 50 mg.

The application is deficient and therefore not approvable under Section 505 of the Act for the following reasons:

1. Your comparative dissolution rate studies and request for bioavailability/bioequivalency waiver is under review by the Division of Bioequivalence. You will be advised when their review is completed.
2. It fails to provide adequate labeling information. In this regard:

Container: Not Satisfactory

The quantity is listed as 100 (1000) tablets  
(rather than capsules).

Insert: Not Satisfactory

In accord with very recent changes, please make the following revisions:

- a. CONTRAINDICATIONS-delete heading-"Use in Lower Respiratory Disease" and the first paragraph following.

Underline the first sentence in the next paragraph  
Antihistamines also are contraindicated in the  
following conditions:

- b. PRECAUTIONS-General

(1) Paragraph one should be changed to read:  
Diphenhydramine hydrochloride has an atropine-like action and therefore should be used with caution in patients with a history of lower respiratory disease including asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease or hypertension.

(2) Drug Interactions-delete CAUTION: Patients taking monoamine oxidase inhibitors should not receive antihistamine therapy concurrently.

- c. DESCRIPTION-structural formula- -N-N-should be in italics.

- d. OVERDOSAGE-underline the following phrases at the beginning of paragraphs 2,3,4 and 5:

If vomiting has not occurred spontaneously...  
If vomiting is unsuccessful...  
Saline cathartics...  
Stimulants....

- e. DOSAGE AND ADMINISTRATION  
Children....three or four times daily....  
(rather than three to four).

Please revise your container labels and package insert labeling, then prepare and submit twelve final printed copies of container labels and draft copy of package insert labeling for our review and comment.

3. For the Components and Composition:

Please include the formula for the capsule in these sections, as shown on page 97.

4. For the active ingredient:

Please identify \_\_\_\_\_ stated as manufacturer on page 78. This name is not otherwise indicated as a source for the active ingredient.

5. For the inactive ingredient:

- a. It fails to specify the botanical source of the Starch, NF used.

- b. It fails to assure that the Starch, NF meets compendial requirements in that the analytical report (page 87) fails to include tests for pH, Residue on Ignition, Iron, Oxidizing substances, Sulfur dioxide and no Certificate of Analysis from the supplier is provided.

6. For the finished drug product:

It should be understood that the USP procedure will be used as the regulatory method. In this connection provide comparative data showing that the \_\_\_\_\_ to the USP assay procedure.

The file is now closed. You are required to take one of the actions described at 21 CFR 314.120 which will either amend or withdraw the application, or if you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

CC:  
HFN-237 2/30/86  
TPoux/CChang/MGoldman/tr/7/29/86  
0936S  
Not Approvable

Marvin Seife, M.D.  
Director  
Division of Generic Drugs  
Office of Drug Standards  
Center for Drugs and Biologics

7-3186

REVIEW OF PROFESSIONAL LABELING

ANDA?DRAFT

DATE OF REVIEW: July 24, 1986

ANDA/NDA#: 89-488 (25 mg)  
89-489 (50 mg)

NAME OF FIRM: Mutual

NAME OF DRUG: Generic: Diphenhydramine Hydrochloride Capsules, USP

DATE OF SUBMISSION: May 9, 1986

COMMENTS:

Container: Not Satisfactory

- A. The quantity is listed as 100 (1000) tablets (rather than capsules).

Insert: Not Satisfactory

In accord with very recent changes, please make the following revisions:

- A. CONTRAINDICATIONS-delete heading-"Use in Lower Respiratory Disease" and the first paragraph following.

Underline the first sentence in the next paragraph  
Antihistamines also are contraindicated in the following  
conditions:

- B. PRECAUTIONS-General

1. Paragraph one should be changed to read:  
Diphenhydramine hydrochloride has an atropine-like action and therefore should be used with caution in patients with a history of lower respiratory disease including asthma, increased intraocular pressure, hyperthyroidism, cardiovascular disease or hypertension.
2. Drug Interactions-delete CAUTION: Patients taking monoamine oxidase inhibitors should not receive antihistamine therapy concurrently.

- C. DESCRIPTION-structural formula- -H-N-should be in italics

- D. OVERDOSAGE-underline the following phrases at the beginning of paragraphs 2,3,4 and 5

If vomiting has not occurred spontaneously...  
If vomiting is unsuccessful...  
Saline cathartics...  
Stimulants....

- E. DOSAGE AND ADMINISTRATION  
Children....three or four times daily....  
(rather than three to four)

RECOMMENDATIONS:

1. Inform the firm of above comments.
2. Request the firm revise their container labels and package insert labeling then prepare and submit twelve final printed copies of container labels and draft copy of package insert labeling for our review and comment.

HFN-238  
T.Poux/sw/7-24-86  
2458A Pg 4-5

/   
Tom Poux

ANDA 89-489

MAY 20 1986

Mutual Pharmaceutical Co.  
Attention: Mr. Suhas Sardesai  
1100 Orthodox Street  
Philadelphia, PA 19124

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for the following:

NAME OF DRUG: Diphenhydramine Hydrochloride Capsules USP, 50 mg

DATE OF APPLICATION: May 9, 1986

DATE OF RECEIPT: May 13, 1986

We will correspond with you further after we have had the opportunity to review the application.

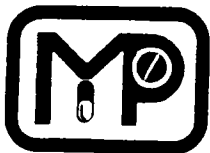
Please identify any communications concerning this application with the NDA number shown above.

Sincerely yours,

m /AR S-20-86  
Marvin Seife, M.D.  
Director  
Division of Generic Drugs  
Office of Drug Standards  
Center for Drugs and Biologics

cc: HFN-230  
Chang  
MSeife/JSturm/jt/5-16-86  
Ack 0183b  
5-19-86





# Mutual Pharmaceutical Company, Inc.

1100 Orthodox Street • Philadelphia, Pennsylvania 19124 • (215) 288-6500

May 9, 1986

Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Standards  
Center for Drugs and Biologics  
Food and Drug Administration  
HFN 230, Rm 16-70  
5600 Fishers Lane  
Rockville, MD 20857

*505(j)(2)(n)  
waiver  
have been met  
2/24/86*

Re: **Abbreviated New Drug Application**  
Product: **Diphenhydramine Hydrochloride Capsules, 50 mg.**

Dear Doctor Seife,

Pursuant to Section 505(j) of the Federal Food Drug and Cosmetic Act, and the Amendments thereto, we are submitting herewith, in duplicate, an abbreviated new drug application for the new drug referred supra.

Included in Section 3 of this application we are respectfully requesting a waiver to conduct bioavailability studies on the dosage form based upon the comparative dissolution rate studies we have conducted on the dosage form of Parke-Davis's Benadryl Capsules 50 mg. Vide: the Orange Section - Pharmacokinetics in Volume No. 2.

Concurrently we are separately filing for the 25 mg potency dosage forms of Diphenhydramine Hydrochloride Capsules.

We respectfully submit the following:

- a. Form 356-H
- b. Volume No. 1 - Copy No. 1 (Blue Folder)
- c. Volume No. 2 - Copy No. 1 (Orange Folder)
- d. Volume No. 1 - Copy No. 2 (Red Folder)
- e. Volume No. 2 - Copy No. 2 (Orange Folder)
- f. Four (4) sets of labels (drafts)

Yours sincerely,  
MUTUAL PHARMACEUTICAL CO., INC.

*Suresh Sardesai*

SURESH SARDESAI, M.S.  
Director of Operations

*May 20 1986  
GENERIC DRUGS*